UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

1CD

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/135,183	08/17/98	BAMDAD C	A-65909-1/RF

HM22/1001

RICHARD F TRECARTIN
FLEHR HOHBACH TEST ALBRITTON AND HERBERT
SUITE 3400
FOUR EMBARCADERO CENTER
SAN FRANCISCO CA 94111-4187

EXAMINER	
LUNDGREN, J	
ART UNIT	**PAPER NUMBER**
1653	5
DATE MAILED:	10/01/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/135,183	Applicant(s) Bamdad
	Examiner Jeffrey S. Lundgren	Group Art Unit 1653

☒ Responsive to communication(s) filed on *Feb 8, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-19* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-19* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement filed on 2/8/99 was considered. References either not supplied, not supplied in English, not supplied beyond the abstract with relevance as it pertains to the application, or not supplied so that the reference can be identified on the Information Disclosure Statement were lined through and not considered. See MPEP § 609 for proper filing procedures and the minimum requirements of an Information Disclosure Statement.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. For

example, see "Example 10" on page 97. Corrections throughout the entire specification are required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 3-4, and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has not specifically identified the term "ETM" in any of the claims. Although the specification defines "ETM" to be the abreviated form of "electron transfer moieties", Applicant must have antecedant basis. Applicant can overcome this rejection by ammending the first claim with the insertion of "(ETM)" immediately after the term electrom transfer moieties.

6. Claims 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is drawn to a composition comprising: 1) an electrode comprising a monolayer comprising conductive oligomers and a capture probe; and 2) a label sequence comprising a first portion (which is capable of hybridizing to "a component of an assay complex") and a second portion comprising a recruitment linker, wherein the recruitment linker does not hybridize to a component of the "assay complex" and comprises at least one covalently attached electron transfer moiety.

It is unclear what applicant is claiming with the use of the term "assay complex". On page 53, line 3 of the specification of the current application, "assay complex" may be interpreted in multiple ways. An individual could reasonably interpret the assay complex to be the equivalent of the recruitment linker, as the applicant has placed the term "the recruitment linker" in parentheses immediately following the term "assay complex". If this is the intended interpretation of the term, then it remains unclear as to how one is to detect the target since the recruitment linker has previously been defined to be part of the "label probe" (page 37, lines 16-22). Furthermore, one could interpret the second sentence beginning on page 53 that uses the term "assay complex", to convey that a critical distance must be maintained for electron transfer, thus the assay complex, and in particular, the recruitment linker which is the critical portion of the assay complex since it contains the ETM, must be in proximity to the electrode. The later of the two interpretations of this rejections is more plausible, however, the term "assay complex" is not clearly defined. What are the components of the assay complex? Is the capture probe,

capture extender probe, target, amplifier, and/or any other hybridized or covalently attached moiety included in the assay complex?

If Examiner has failed to identify Applicant's definition of "assay complex" from the specification as it pertains to this rejection over claims 2-10, Applicant is advised to specifically point to the defining subject matter from the specification (i.e., page and line number(s)).

Claims 3-10 are rejected on the aforementioned grounds, as the claims are dependent on claim 2.

7. Claims 11-12, and 16-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is drawn to a method of detecting a target nucleic acid sequence, wherein the target is "attached" to an electrode comprising a monolayer of oligomers. However, Applicant has not specifically claimed the method of attaching the target oligonucleotide to the electrode surface (i.e., hybridization, covalent attachment, physisorption, etc.). Also, it is not clear whether Applicant claiming attachment of the target through a capture probe or possibly a capture probe extender.

Claims 12, and 16-19 are rejected on the aforementioned grounds, as the claims are dependent on claim 11.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meade et al. (U.S. Patent No. 5,591,578), and Ihara et al. (Chem Commun., pages 1609-1610 (1997)), in view of Collins et al. (U.S. Patent No. 5,780,224, Jul. 14, 1998).

Meade et al., disclose a composition and a method for the detection of a target nucleic acid by the "molecular wire" concept comprising the hybridization of at least a target DNA with a capture DNA, wherein the hybridized complex comprises electron transfer moieties (ETMs), of which there is at least an electron donor and acceptor. In claim 10, Meade et al., claim:

> "10. A method of detecting a target sequence in a nucleic acid sample comprising:
> a) hybridizing a single stranded nucleic acid containing one or multiple electron donor moieties and one or multiple electron acceptor moieties to said target sequence to form a hybridization complex, wherein one of said electron donor or acceptor moieties is an electrode and the other is a transition metal complex covalently attached to the 2' or 3' position of a ribose of the ribose-phosphate backbone of said nucleic acid, wherein said transition metal is selected from the group consisting of Cd, Mg, Cu, Co, Pd, Zn, Fe and Ru; and
>
> b) detecting electron transfer between said electron donor moieties and said electron acceptor moieties in the hybridization complex as an indicator of the presence or absence of said target sequence. "

Meade et al., meet the limitations of an electrode comprising a monolayer of conductive oligomer capture probes since the single-stranded nucleic acid of claim 10 (i.e., capture probe) that hybridizes to the target nucleic acid, and contains the electron donors/acceptors.

Meade et al., do not teach a method or composition where the capture probe specifically does not contain the ETM, or all of the possible probe/target arrangements.

Ihara et al., teach a method for detecting a target nucleic acids, whereby an electrode with monolayers of oligomers serve as capture probes for the target and do not contain ETMs. The target DNA comprises the first region complementary to the capture probe, and a second region that does not hybridize to the capture probe and comprises an attached electron transfer moiety (i.e., a hybridized label containing the ETM; see page 1609).

Collins et al., disclose using a capture probe and a capture probe extender (first series probes) capable of binding all plurality of target nucleic acids to spatially distinct supports (column 7, third full paragraph).

From the teachings of the combined references involving the detection of target nucleotide sequences based on the "molecular wire" principle, it is obvious that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. One of ordinary skill in the art would have been motivated to combine the teachings of Meade et al., with the teachings of Risser et al., to produce a method/composition for detecting target nucleic acids with electrode-immobilized capture probes, with a target DNA with a first region hybridized to the capture probe and a second region comprising and ETM. One would have been motivated to combine the teachings of Collins et al., with the teachings of Meade et al., and Ihara et al., to extend the layers of the oligonucleotides on the sensing substrate (i.e., electrode) as a means of enabling the capture probe (or a capture probe extender) to selectively

hybridize with the target nucleic acid, and then bind label probe(s). Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

10. No claims are allowable.

11. Additionally, art relevant to the current application, incorporated by reference herein, is the first disclosure of Nilsen et al. (U.S. Patent No. 5,487,973, Jan. 30, 1996) and the second disclosure of Nilsen et al. (U.S. Patent No. 5,175,270, Dec. 29, 1992). Nilsen et al. (first cited disclosure), disclose a method where a multiplicity of oligomers are used to "build" upon substrates in order to provide a method for detecting the target nucleic acid (see abstract). The teachings of Nilsen et al., provide the art with the means to extend the target-capture chemistries beyond conventional assays with only a primary, immobilized, oligonucleotide-hybridization probe. Nilsen et al., also demonstrate two different types of capture probes, which act as a bridge, one binding a first segment of the target, a second binding a second segment of the target (column 14, second full paragraph; see Figure 5). The advantages of Nilsen et al., are useful when one is limited by the chemistries where a signal probe may not be able to be directly incorporated with the capture or target-identifier. Nilsen et al., also disclose the advantage of signal enhancement through the use of a "signal amplifying components" (i.e., oligo-dendrimers).

These amplifying components of the invention add multiple "signaling-moieties" only in the presence of the target and function as an extension of the capture elements.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeffrey S. Lundgren whose telephone number is (703) 306-3221. The Examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM (EST).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Bradley Sisson, can be reached at (703) 308-3978.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1653 via the PTO Fax Center using (703) 305-3014 or 305-4227. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

9/23/99

Jeffrey S. Lundgren, Ph.D.

Eggerton Campbell

EGGERTON A. CAMPBELL
PRIMARY EXAMINER